REMARKS

Claims 31-32, 34-40, 42-49 and 53-59 currently appear in this application. The Office Action of September 14, 2004 has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claims 31-32, 36, 41-43, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley et al.

This rejection is respectfully traversed. Holmes-Farley et al. disclose poly(allylamine) hydrochloride crosslinked with epichlorohydrin in a mixed medium of water and acetonitrile. However, Holmes-Farley et al. neither teach nor suggest the use of such a crosslinked polymer formulated as tablets. All of the tests showing pharmacological activities were conducted with the polymer formulated as capsules. Accordingly, Holmes-Farley et al. do not suggest the use of the poly(allylamine) crosslinked with epichlorohydrin in a mixed medium of water and acetonitrile for formulating into tablets.

Thus, Holmes-Farley et al. do not suggest that their formulation has the desirable physical properties as the have

the tablets of the present invention, such as high hardness. One skilled in the art reading Holmes-Farley et al. could not reasonably expect to achieve any success in formulating tablets having the desired physical properties that are achieved by the present invention. Moreover, Holmes-Farley et al. only confirmed the desired pharmacological effects by using the polymer in the form of capsules. Therefore, there is no motivation in Holmes-Farley et al. to use the polymer for preparing tablets.

Claims 33-49 and 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley et al. in view of Sato et al. The Examiner concedes that Holmes-Farley do not specify crystalline cellulose or HPC as excipients. Sato has been cited for a teaching that in molding pharmaceutical compositions into tablet formulations, many conventional carriers can be used, such as lactose, sucrose, microcrystalline sucrose, etc., and conventional disintegrators such as low-substituted HJPC.

This rejection is respectfully traversed. The claims have now been amended to recite the hardness of the tablets claimed. Support for this can be found in the specification as filed, wherein tablets prepared from a mixture of the polymer with an additive of crystalline cellulose (Example 2) exhibited a hardness higher than that

prepared from the polymer alone (Example 1) under the same compression conditions. The use of the additive increases the actual application of the polymer in the form of a tablet.

One skilled in the art appreciates that it is important to choose a specific additive to provide tablets having desired physical properties, and to reduce a surface stickiness of the tablet to thereby produce tablets having appropriate properties.

The phosphate-binding polymer of the present invention has unique properties, such as high hygroscopicity and swelling properties. This polymer also provides poor tablet hardness when processed into tablets simply by compressing the polymer.

Patients undergoing dialysis to whom the phosphate-binding polymers are to be administered as remedies for hyperphosphatemia are frequently subject to a restricted intake of water, and phosphate-binding polymers are usually taken in a relatively large single dose, *i.e.*, from 1-2 grams. Thus, it is important to provide a preparation with a high concentration of the active component, *i.e.*, a low concentration of additive, so as to reduce the size of the tablets so that the tablets are as small as possible. Given these requirements, appropriate formulation of the phosphate-binding polymer into tablets had hereto proved to

very difficult. Further, it was necessary to reduce surface stickiness of tablets formulated from the polymer and an additive in order to improve ease or oral administration, and to solve problems such as insufficient hardness and undesirable stickiness of tablets upon formation.

As stated above, the phosphate-binding polymer has high swelling properties and thus, by absorbing water, it rapidly swells to become a gel having a remarkably high degree of stickiness. Consequently, when the phosphate-binding polymer is administered orally, the polymer absorbs saliva in the oral cavity, which produces a sticky gel which is very difficult to swallow unless taken with great quantities of water. However, as stated above, patients undergoing dialysis to whom the phosphate-binding polymers are to be administered as remedies for hyperphosphatemia, are frequently subjected to restricted intake of water. Therefore, the polymer *per se* is not an appropriate drug for treating patients with hyperphosphatemia, since it is necessary that the patient ingest a large amount of water when the polymer is administered orally.

The phosphate-binding polymer for treating hyperphosphatemia is administered in a single dose of about 1-2 grams. Patients to be treated include a high proportion of elderly persons, who tend to have difficulty swallowing

tablets. Thus, it is important to reduce the stickiness of the tablets containing the polymer when they contact oral mucosa. In addition, when coating uncoated tablets with a thin film to prepare coated tablets, it is also important to reduce the stickiness of uncoated tablets of phosphate-binding polymer to prevent production of twin tablets composed of two tablets adhered to each other, or non-uniform coatings. This is a problem with the phosphate-binding polymer of the present invention, which is cross-linked and insoluble in water, yet it absorbs water and swells to become a very sticky gel.

According to the present invention, the phosphate-binding polymer can be formulated into tablets using a specific additive such as crystalline cellulose, low substituted hydroxypropyl cellulose (HPC) or a mixture thereof to provide tablets with sufficient hardness, improved disintegration and low abrasion loss, as well as a reduced stickiness. Since the phosphate-binding polymer tablets prepared according to the present invention are prevented from swelling in the oral cavity and from adhering to oral mucosa upon administration, they can be administered orally with significant ease, and then they rapidly disintegrate and disperse in the stomach to bind phosphate efficiently. Consequently, the tablets of the present invention can be orally administered to patients with hyperphosphatemia who are

subject to a restricted intake of liquid, and the tablets therefore have improved clinical applicability as medicines.

Furthermore, according to the present invention, stickiness between uncoated tablets is reduced, and therefore, formulation into tablets is made easy, which makes it possible to produce high quality tablets. The reduction of stickiness is shown in the test data of the declaration submitted herewith.

Sato et al. disclose many additives used to formulate succinic acid compounds. These succinic acid compounds are completely different in chemical and physical structures and pharmacological activity form the phosphate-binding polymer. Sato et al. disclose a large number of conventional additives. However, the additives for the phosphate-binding polymer must be carefully chosen to provide unexpectedly good effects. For this reason, it is respectfully submitted that one skilled in the art reading Holmes-Farley et al. and Sato et al. would not be motivated to select the particular additives that minimize the stickiness of the phosphate-binding polymer.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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